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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 12/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,036	THASTRUP ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment submitted 9/9/2005 has been received and entered. After entry of the amendment, claims 44-54 are pending and under examination.

New Grounds of Rejection

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 44-54 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-5, 31-36, 41, 54, and 58-61 of prior U.S. Patent No. 6,518,021. **This is a new rejection necessitated by applicants' amendments to the claims.** This is a double patenting rejection.

Claims 1, 2, and 36 of the '021 patent recite the same method steps as the independent instant claims 44, 45, and 46 respectively. The preambles of the instant claims 44 and 45 have been amended to recite methods for detecting " a biologically active substance by detecting intracellular translocation of a subunit of a component of an intracellular pathway". The preamble of claim 46 reads as above, except the subunit is "of a biologically active polypeptide affecting intracellular processes". The above underlining indicates language different than that of claims 1, 2, and 36 of '021. The "biologically active substance" language is found in step (b) of claims 1, 2, and 36: i.e. "incubating...with a substance to be screened for biological function or

biological effect", and thus this language has been merely duplicated from a method step of the patented claims to the preamble of the instant claims. Therefore, the methods of the '021 patent detect "biologically active substance(s)", particularly in light of claim 54, which recites a method according to claims 1, 2, or 36 that is a screening method for a "biologically active substance". Regarding detecting "a subunit of a component" (as in the instant claims) rather than detecting "a component" (as in the patented claims), the terms are coextensive in scope. For example, detecting the translocation of a component necessarily detects translocation of a subunit of the component, and vice versa. See Example 1 (catalytic subunit of cAMP dependent protein kinase), Example 11 (alpha subunit of human IkappaB kinase), and Example 15 (p85alpha regulatory subunit of PI3-kinase) of the '021 patent and the instant specification wherein the above subunits were tagged with GFP and used to detect translocation of the component. Finally, steps (c) in claims 44-46 have been amended to add language that refers back to the preamble of the claims: "and said translocation being indicative that said substance to be screened is biologically active". This language adds no new process steps or compositions to the claimed methods, and does not change the scope of the claimed methods relative to the methods of claims 1, 2, and 36 (respectively) of the '021 patent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 44-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Carey et al (J. Cell Biol., June 1996, cited by applicants in the IDS of 2/5/2002). **This is a new rejection necessitated by applicants' amendments to the claims.**

The claims recite methods for detecting a biologically active substance by detecting intracellular translocation of a subunit of a component of an intracellular pathway (claims 44 and 45) or of a biologically active peptide affecting intracellular processes (claim 46). The recited method steps are: (a) culturing cells containing a nucleotide sequence coding for a hybrid polypeptide comprising a luminophore linked to the subunit; (b) incubating the cells with a substance to be screened for biological activity; (c) measuring the light emitted from the luminophore and determining a result or variation (claims 44 and 46) or (c) extracting quantitative information relating to the translocation of the subunit by recording variation in spatially distributed light emitted from the luminophore (claim 45); and (claim 46 only) (d) measuring the effect of said substance on inhibition/activation of enzymatic activity of the subunit. The method of claim 45 may be based on recordings according to a predetermined calibration. In claims 44-46, the substance may be a chemical substance or may be a substance whose affect on the intracellular pathway is to be determined. The intracellular pathway may be a signaling pathway. The luminophore may be a fluorophore, which may be GFP.

Carey et al disclose a fusion protein of glucocorticoid receptor and GFP (GR-GFP) that was transfected into BHK21 cells hat were treated with dexamethasone to determine the effect of dexamethasone on the translocation GR-GFP fusion protein from the cytoplasm into the nucleus (see abstract and Fig. 1). The measurement of translocation was done by determining a "variation" of GR-GFP location (either cytoplasmic or nucleic) and quantitated by recording

microscopic images followed by analysis of the images with Cosmos software (see section entitled "Microscopy", second column, page 986). Dominant negative mutants of the enzyme Ran/TC4 GTPase (Ran) were used to identify wild-type Ran as responsible for nuclear import of the GR-GFP protein (see abstract, paragraph bridging first and second columns page 986, and last paragraph, first column, page 994). Thus, Ran/GR-GFP is a component of the glucocorticoid receptor signaling pathway, with Ran and GR-GFP being subunits of the component.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carey as applied to claims 44-52 above, and further in view of Cormack et al (Gene, 1996). **This is a new rejection necessitated by applicants' amendments to the claims.**

The claims are described above, except the GFP may have an F64L mutation, or be selected from the group of GFPs listed in claim 54.

The teachings of Carey et al are described above and applied as before.

Cormack et al teach mutations of GFP, including the F64L and S65T (Table 1) substitutions in GFPmut1, which had a 35-fold increase in fluorescence intensity relative to wt GFP (Table II, page 37). Cormack et al teach these GFP mutants to have wide applicability in any GFP study (page 38, first column, number (4)), that they fluoresce more intensely, and are more stable due to efficient folding (abstract and paragraph linking pages 33 and 34).

The claimed methods are essentially disclosed by Carey et al with the exception of the GFP F64L substitution. The ordinary skilled artisan, seeking a method to detect translocation of GFP-tagged subunits would have been motivated to use GFP F64L/S65T substitution (or the other GFP mutants) with the detection methods of Carey et al because Cormack et al teaches them to be well known types of GFP proteins that have utility for detection in cell culture and to have superior fluorescence and stability properties. It would have been obvious for the skilled artisan to do this because of the known benefit of using a GFP protein with superior fluorescence and stability as taught by Cormack et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 46, 48-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 46 recites the limitation "enzymatic activity" in the last two lines. There is insufficient antecedent basis for this limitation in the claim. This rejection affects all dependent claims.

Claim Objections

Claim 48 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 48 recites that the substance to be screened in claims 44-46 may be a chemical substance. Absent evidence to the contrary, all substances to be screened must be chemical substances, i.e. they are composed of atoms. There appears to be no instance where a substance to be screened is not a chemical substance.

Conclusion

Any rejection not repeated in this Office Action is withdrawn.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1633

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